

Adalimumab (Humira®)

This sheet is about exposure to adalimumab in pregnancy and while breastfeeding. This information should not take the place of medical care and advice from your healthcare provider.

What is adalimumab?

Adalimumab is a medication that has been used to treat autoimmune diseases such as rheumatoid arthritis, psoriatic arthritis, plaque psoriasis, ankylosing spondylitis, and ulcerative colitis. Adalimumab is called a tumor necrosis factor (TNF) inhibitor because it binds and blocks TNF. TNF is a substance in the body that causes inflammation in the joints, spine, and skin. Adalimumab is sold under the brand name Humira®.

I am taking adalimumab, but I would like to stop taking it before getting pregnant. How long does the drug stay in the body?

People eliminate medication at different rates. In healthy adults, it takes up to 12 weeks (3 months), on average, for most of the adalimumab to be gone from the body. There is one case report of person who stopped adalimumab at week 16 of their pregnancy. Medication levels were found in their blood and the umbilical cord blood at time of delivery 21 weeks later.

I take adalimumab. Can it make it harder for me to get pregnant?

Based on the studies reviewed, it is not known if adalimumab can make it harder to get pregnant. There are no reports linking adalimumab to fertility problems. Adalimumab is being studied to see if it may be used with other therapies to improve the success rates of certain fertility treatments.

Does taking adalimumab increase the chance for miscarriage?

Miscarriage can occur in any pregnancy. Based on the studies reviewed, it is not known if adalimumab can increase the chance for miscarriage. Available information does not suggest an increased chance for miscarriage in people exposed to adalimumab or another TNF inhibitor during pregnancy.

Does taking adalimumab increase the chance of birth defects?

Every pregnancy starts out with a 3-5% chance of having a birth defect. This is called the background risk. Seven studies reporting on the outcomes of almost 700 pregnancies with exposure to adalimumab found no increased chance for a pattern of birth defects. Also, there have been several case reports of babies born without birth defects or other problems after being exposed to adalimumab during pregnancy.

A study published in 2009 looked at birth defects reported in 41 people who used a TNF inhibitor during pregnancy. This study did not include adalimumab. The authors suggested these medications could cause VACTERL association. VACTERL association is a pattern of birth defects that includes vertebral (spine), anal, cardiac (heart), tracheal-esophageal (structures in the neck), renal (kidney), and limb (arms and legs) defects. Two or more defects in this pattern must be found for a baby to be diagnosed with VACTERL. Also, other syndromes or genetic disorders must be ruled out before a diagnosis of VACTERL can be made. Due to the study design, limited data, and voluntary reporting, this review does not support the conclusion that TNF inhibitors cause an increased chance for a pattern of birth defects.

One study among 495 people taking a TNF inhibitor (147 used adalimumab) for an autoimmune disease reported a slightly higher chance for a birth defect. The study compared these pregnancies to the pregnancies of people who did not have an autoimmune disease. It is not clear if the medication or the underlying disease caused the slightly higher chance.

In summary, studies looking at adalimumab use during pregnancy have not shown an increased chance for a pattern of birth defects. It is also reassuring that a large amount of adalimumab is not thought to reach the pregnancy during the first trimester.

Does taking adalimumab in pregnancy increase the chance of other pregnancy-related problems?

Information on the use of adalimumab in the third trimester is limited. More adalimumab is thought to cross the placenta during the third trimester than in the first trimester. There have not been any reports that have shown risks to a pregnancy when a person takes adalimumab in the third trimester. One study reported no increased chance of infections in baby's first year.

There are no official recommendations for using adalimumab in the third trimester. The decision to use adalimumab in the later part of pregnancy may be based on your condition and how serious your symptoms are. Talk with your healthcare provider about the best way to treat your condition.

Does taking adalimumab in pregnancy affect future behavior or learning for the child?

Based on the studies reviewed, it is not known if adalimumab increases the chance for behavior or learning issues.

Can my baby receive live vaccines before one year of age if I take adalimumab later in pregnancy?

Most vaccines given in the first 6 months of life are noninfectious and can be given to a baby even if adalimumab is present in his/her blood. Noninfectious vaccines are not live vaccines, meaning a person cannot get the infection from the vaccine. Live vaccines always carry a small chance a person could contract the infection from the vaccine. However, live vaccines usually contain a milder form (attenuated) of the virus or bacteria than what you might be exposed to in the community. Types of live vaccines include measles-mumps-rubella (MMR), varicella (chicken pox), and rotavirus vaccine. The rotavirus vaccine is the only live vaccine given to infants less than one year of age in the United States (US). Rotavirus is one of the leading causes of vomiting and severe diarrhea in children. The rotavirus vaccine is usually recommended for infants in the US, and is the best way to protect infants against rotavirus disease.

There is a single report of a person treated with another TNF inhibitor (infliximab) during pregnancy whose infant received a live BCG vaccine (to prevent tuberculosis) at 3 months of age. The baby later died of a suspected BCG infection. It is not known if exposure to infliximab was related to the baby's death. This vaccine is used in countries where tuberculosis infections are common and is not usually given in the US.

While live vaccines are usually not given to those using TNF inhibitors like adalimumab, vaccines protect babies from getting common infections that can sometimes cause serious or even life-threatening illness in young children. Be sure to let your pediatrician know of any medications or exposures you had during pregnancy or breastfeeding, including treatment with TNF inhibitors. Your pediatrician can discuss the risks and benefits of live vaccines with you.

Breastfeeding while taking adalimumab:

Available data suggests that adalimumab levels in breast milk are very low. There are a small number of reports of healthy newborns who were exposed to adalimumab through breastmilk. Adalimumab is usually not well absorbed by the gut, so the amount of the medication absorbed by the baby is expected to be low. If you suspect that the baby has symptoms (vomiting, frequent infections), contact the child's healthcare provider. Be sure to talk to your healthcare provider about all of your breastfeeding questions.

If a male takes adalimumab, could it affect fertility (ability to get partner pregnant) or increase the chance of birth defects?

Based on the studies reviewed, adalimumab is not expected to negatively affect fertility or increase the chance of birth defects above the background risk. In general, exposures that fathers or sperm donors have are unlikely to increase the risks to a pregnancy. For more information, please see the MotherToBaby fact sheet Paternal Exposures at <https://mothertobaby.org/fact-sheets/paternal-exposures-pregnancy/>.

MotherToBaby is currently conducting studies looking at autoimmune diseases and the medications used to treat these diseases in pregnancy. If you are interested in taking part in one of these studies, please call 1-877-311-8972 or sign up at <https://mothertobaby.org/join-study/>.

Selected References:

- Ben-Horin S, et al. 2010. Adalimumab level in breast milk of a nursing mother. *Clin Gastroenterol Hepatol*;8:475-6.
- Burmester GR, et al. 2017. Adalimumab long-term safety: infections, vaccination response and pregnancy outcomes in patients with rheumatoid arthritis. *Ann Rheum Dis*. 76(2):414-417.
- Bröms G, et al. 2016. Low risk of birth defects for infants whose mothers are treated with anti-tumor necrosis factor agents during pregnancy. *Clin Gastroenterol Hepatol* 14(2):234-241.
- Carter JD, et al. 2009. A safety assessment of tumor necrosis factor antagonists during pregnancy: a review of the Food and Drug Administration database. *The Journal of Rheumatology* 36:3.
- Carter JD, et al. 2006. Tumor necrosis factor-alpha inhibition and VATER association: a causal relationship. *J Rheumatol* 33(5):1014-7.
- Chambers CD, et al. 2019. Birth outcomes in women who have taken adalimumab in pregnancy: A prospective cohort study. *PLoS One* 14 (10)
- Clark DA. 2010. Anti-TNFalpha therapy in immune-mediated subfertility: state of the art. *J Reprod Immunol*. 85(1):15-24.
- Diav-Citrin O, et al. 2014. Pregnancy outcome following gestational exposure to TNF-alpha-inhibitors: A prospective, comparative, observational study. *Reprod Toxicol*; 43: 78-84.
- Fritzsche J, et al. 2012. Infliximab and adalimumab use during breastfeeding. *J Clin Gastroenterol*; 46:718-9.
- Hoxha A, et al. 2017. Pregnancy and fetal outcomes following anti-tumor necrosis factor alpha therapy: A prospective multicenter study. *Joint Bone Spine* 84(2):169-173.
- Johansen CB, et al. 2018. The use and safety of TNF inhibitors during pregnancy in women with psoriasis: A review. *Int J Mol Sci*. 19(5):1349
- Julsgaard M, et al. 2013. Adalimumab levels in an infant. *J Crohns Colitis*;7(7):597-8.
- Kawai Y, et al. 2019. Pregnancy outcomes of patients exposed to adalimumab in Japan. *Dig Dis* 37(2): 123-130.
- Leung Y, et al. 2014. Management of the pregnant inflammatory bowel disease patient on anti-tumor necrosis factor: state of the art and future directions. *Can J Gastroenterol Hepatol*; 28(9):505-9.
- Lund T, et al. 2016. Use of TNF-inhibitors and ustekinumab for psoriasis during pregnancy: A patient series. *Derm Therapy*. May; 30 (3)
- Mahadevan U, et al. 2019. Inflammatory bowel disease in pregnancy clinical care pathway: A report from the American Gastroenterological Association IBD parenthood project working group. *Gastroenterology* 156:1508-1524
- Matro R, et al. 2018. Exposure concentrations of infants breastfed by women receiving biologic therapies for inflammatory bowel diseases and effects of breastfeeding on infections and development. *Gastroenterology* 155:696-704
- Micu MC, et al. 2014. TNF-alpha inhibitors do not impair sperm quality in males with ankylosing spondylitis after short-term or long-term treatment. *Rheumatology (Oxford)*. Jul;53(7):1250-5.
- Mishkin DS, et al. 2006. Successful use of adalimumab (Humira) for Crohn's disease in pregnancy. *Inflamm Bowel Dis*. 12:827-828.
- Picardo S, et al. 2019. A pharmacological approach to managing inflammatory bowel disease during conception, pregnancy and breastfeeding: Biologic and oral small molecule therapy. *Drugs* 79:1053-1063.
- Ramonda R, et al. 2014. Influence of tumor necrosis factor alpha inhibitors on testicular function and semen in spondyloarthritis patients. *Fertil Steril*; 101(2):359-65.
- Roux CH, et al. 2006. Pregnancy in rheumatology patients exposed to anti-tumour necrosis factor (TNF)-{alpha} therapy. *Rheumatology* 46:695-698.
- Schnitzler F et al. 2011. Outcome of pregnancy in women with inflammatory bowel disease treated with antitumor necrosis factor therapy. *Inflamm Bowel Dis*. 17(9):1846-54.

- Villiger PM, et al. 2010. Effects of TNF antagonists on sperm characteristics in patients with spondyloarthritis. *Ann Rheum Dis* 69(10): 1842-4.
- Viktil KK, et al. 2012. Outcomes after anti-rheumatic drug use before and during pregnancy: a cohort study among 150 000 pregnant women and expectant fathers. *Scandinavian Journal of Rheumatology*, 41(3): 196-201
- Weber-Schoendorfer C, et al. 2015. Pregnancy outcome after TNF- α inhibitor therapy during the first trimester: a prospective multicentre cohort study. *Br J Clin Pharmacol*.
- Winger EE et al., 2011. Birth defect rates in women using adalimumab (Humira®) to treat immunologic-based infertility in IVF patients. *Am J Reprod Immunol*. 66(3):237-41.